

Diagnosis and Management of First Case of COVID-19 in Canada: Lessons Applied From SARS-CoV-1

Xavier Marchand-Sénécal,¹ Rob Kozak,¹ Samira Mubareka,^{1,2} Natasha Salt,¹ Jonathan B Gubbay,³ Alireza Eshaghi,³ Vanessa Allen,^{2,3} Yan Li,⁴ Natalie Bastien,⁴ Matthew Gilmour,⁴ Omar Ozaldin,⁵ and Jerome A. Leis^{1,6}

¹Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada, ²Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada, ³Public Health Ontario Laboratory, Toronto, Ontario, Canada, ⁴National Microbiology Laboratory, Public Health Agency of Canada, Winnipeg, Manitoba, Canada, ⁵Communicable Disease Control, Toronto Public Health, Toronto, Ontario, Canada, and ⁶Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

(See the Editorial Commentary by Maxwell on pages 2215–7 and the Brief report by Bryson-Cahn et al on pages 2211–4.)

We report diagnosis and management of the first laboratory-confirmed case of coronavirus disease 2019 (COVID-19) hospitalized in Toronto, Canada. No healthcare-associated transmission occurred. In the face of a potential pandemic of COVID-19, we suggest sustainable and scalable control measures developed based on lessons learned from severe acute respiratory syndrome.

Keywords. COVID-19; 2019-nCoV; SARS-CoV-2; Coronavirus; Infection Prevention.

On 31 December 2019, China alerted the World Health Organization about a cluster of cases of pneumonia of unknown origin in Wuhan, Hubei, China [1]. One week later, a novel coronavirus (provisional name: 2019-nCoV; definitive name: SARS-CoV-2) was identified as the causative agent of the coronavirus disease 2019 (COVID-19). As of 28 February 2020, the outbreak has spread due to human-to-human transmission throughout China and to over 50 countries [2].

Although the majority of transmission has occurred in community settings, super-spreading events in healthcare settings have already been described. In a Wuhan hospital, a nosocomial acquisition is suspected among 29% of healthcare workers (HCW) and 12.3% of the 138 hospitalized patients infected [2]. A patient admitted with unrecognized symptoms of the infection was reported to transmit the virus to >10 HCWs [2]. Healthcare-associated transmission is already described across many other countries including South Korea and Italy.

Our hospital in Toronto, Canada, has past experience caring for patients with SARS-CoV-1 during 2002–2003, where the majority of cases were healthcare-associated [3]. We now report the first imported case of COVID-19 hospitalized in Canada while emphasizing the control measures applied based on lessons learned from severe acute respiratory syndrome (SARS).

CASE PRESENTATION

On 23 January 2020, a 56-year old man presented to our hospital emergency department in Toronto with a new onset of fever and nonproductive cough following return from Wuhan, China, the day prior [4]. The cough began during travel, but the patient only developed fever on the day of presentation, which prompted him to proceed to the emergency department. On clinical assessment, the patient remained well without ever requiring supplemental oxygen. The chest X-ray confirmed the presence of pneumonia [4]. Based on high suspicion for COVID-19, throat and midturbinate swabs (FLOQ Swab by Copan, with UTM transport media) were collected. The patient was admitted to hospital for close observation and supportive management, considering early reports of respiratory failure due to COVID-19 [1]. The specimens collected were negative for influenza A and B, parainfluenza, respiratory syncytial virus, adenovirus, and human metapneumovirus viruses. Coronavirus was detected in both midturbinate and throat swab by pancoronavirus RNA dependent RNA polymerase (RdRp) polymerase chain reaction (PCR) and confirmed as SARS-CoV-2 by sequencing [5].

On the inpatient unit, the patient remained stable. Symptom duration and viral studies are summarized in Figure 1. Following resolution of fever, the patient was discharged home on day 8 of hospital stay. Public health followed up with his wife at home who had cough only. She was also confirmed to have COVID-19. Both patients recovered fully with home isolation, which was discontinued 20 February following 2 negative swabs (the second being day 27 from symptom onset).

DIAGNOSTIC TESTING

All specimens were received at Public Health Ontario Laboratory and eluted in universal transport media (Copan, Brescia, Italy). Total nucleic acid extraction of all primary specimens was performed using a NucliSens easyMAG extraction system instrument (bioMérieux Canada Inc., Québec, Canada), according to the manufacturer's instructions. Reverse transcription and endpoint PCR was performed using hemi nested pan-CoV primers targeting the RdRp [5], and additional primers from this protocol were adapted to be

Received 13 February 2020; editorial decision 1 March 2020; accepted 3 March 2020; published online March 9, 2020.

Correspondence: J. A. Leis, Sunnybrook Health Sciences Centre B103, 2075 Bayview Avenue Toronto, Ontario, Canada M4N 3M5 (Jerome.Leis@sunnybrook.ca)

Clinical Infectious Diseases® 2020;71(16):2207–10

© The Author(s) 2020. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com. DOI: 10.1093/cid/ciaa227

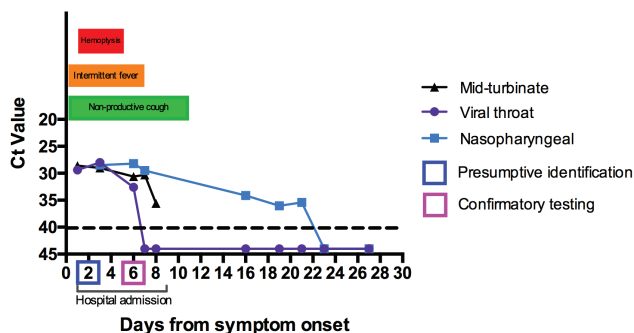


Figure 1. Clinical trajectory and viral shedding of first confirmed case of coronavirus disease 2019. Timeline chart illustrates the symptoms duration and the Ct values of the real-time RT-PCR evolution. Lower Ct values indicate higher viral loads. Abbreviations: Ct, cycle threshold; RT-PCR, reverse-transcription polymerase chain reaction.

SARS-CoV-2 specific. Once validated for clinical testing, specimens were also tested using a published real-time PCR protocol targeting the envelope (E) and nucleoprotein (N) genes [6]. Presumptive confirmation was obtained on day 2 of hospital stay after detection of 2 gene targets by real-time PCR, or PCR and Sanger sequencing of the RdRp gene. Confirmation was conducted by the National Microbiology Laboratory (NML) of the Public Health Agency of Canada by using a real-time PCR assay targeting the N gene (developed at NML). Conventional RT-PCR assay targeting the RdRp was modified from elsewhere [7], and ORF3a (developed at NML) was also performed. Nucleotide analysis of the partial gene sequences of RdRp and ORF3a amplicons showed that they were more closely related to COVID-19 virus.

INFECTION PREVENTION AND CONTROL MANAGEMENT

Based on presence of respiratory symptoms and travel history elicited at triage, this patient was immediately placed in private negative pressure room with airborne-droplet-contact precautions as per our screening protocol for novel high-consequence pathogens. The personal protective equipment (PPE) used included a long-sleeved gown, a pair of gloves, a fit-tested N95 respirator, and a face shield. The patient was cared for by the usual medical and nursing teams in the emergency department and on the unit. Because the PPE used is familiar to our hospital staff and no additional components used (eg, hood or powered air-purifying respirator), no specific training was undertaken other than periodic audits to ensure correct donning and doffing technique.

Additional administrative control measures were put in place given the inherent risks of a novel high-consequence pathogen. First, we maintained a log of each healthcare worker involved in the patient's care. Second, we limited the number of individuals entering the isolation room to the most essential healthcare

workers. For example, no visitors were allowed for the patient who were instead provided the option of using telephone communication. Disposable trays were used to avoid the need to enter and collect food items. Third, all equipment including vital signs machine were dedicated to this patient only. Finally, the critical care and code blue team were alerted on admission of the patient location and the need to abide to hospital policy for minimizing the risks of aerosol-generating medical procedures (AGMP). It was agreed upon by the clinical teams that should the patient require increasing supplemental oxygen, there would be a low threshold to intubate using controlled and protected procedures including use of paralytics, video laryngoscopy, and PPE including N95 masks [8].

Following the patient's discharge, terminal cleaning of the patient's room was completed twice using 0.5% hydrogen peroxide. An IPAC professional and an environmental services supervisor audited both stages of the room cleaning. The list of 32 healthcare workers involved in the patient's care was shared with occupational health and safety, who were to immediately notify IPAC of any new reported specific or nonspecific influenza-like illness within 14 days of discharge. By 28 February 2020, there were no probable or confirmed cases of COVID-19 among other patients or healthcare workers in the facility.

DISCUSSION

We report a case of COVID-19 that was identified immediately, and using transmission-based precautions, monitoring, and administrative controls was safely cared for with no healthcare associated transmission.

Although we expect many more cases of COVID-19 as this epidemic evolves, this first case highlights significant progress made since the SARS outbreak in our own hospital back in 2003. There were 375 cases of SARS throughout Toronto during this prior outbreak, of which 271 resulted from healthcare-associated transmission [3]. Following this event, additional resources in IPAC and public health were instituted in Canada to improve preparedness for managing high-consequence pathogens [9, 10]. The key differences in preparedness and capacities at our hospital between SARS and COVID-19 epidemics are summarized in Table 1.

Additional lessons learned were applied in the management of this patient with COVID-19. First, we did not rely on a specific dedicated team but instead built on IPAC capacities already in place among our usual staffing model that includes baseline preparedness of management of novel high-consequence pathogens. This approach differed from SARS as well as Ebola in 2014, where many hospitals developed dedicated teams to care for these patients, which required significant investments in human resources and training [11]. In the aftermath of those epidemics, this approach was difficult to sustain for hospitals resulting in loss of preparedness. Second, what allows our hospital to maintain

Table 1. Differences Between 2003 and 2020 in Preparedness for a Novel Coronavirus at a Large Academic Hospital in Toronto, Canada.

	2003: SARS in Toronto ^a	2020: COVID-19 Toronto case
Public health structures and infrastructures		
Adequate funding and human resources	No	Yes ^b
Protocols for information sharing among different levels of government	No	Yes
Link between public health and hospitals	Weak, fragmented, uncoordinated	Coordination and information sharing present
Rapid and accurate diagnostic testing	No	Yes
IPAC program structure and related hospital program		
ICP staffing level	Understaffed 3 ICPs for 1257 total beds (0.23 ICP/100 beds)	Adequate 13 ICPs for 1355 total beds (0.96 ICP/100 beds)
ICP certification (Certification Board of Infection Control and Epidemiology)	Not universal	Required
Occupational Health & Safety	Disconnected from IPAC	Coordinated with IPAC
IPAC administrative controls		
Syndromic triage in ED	No	Yes
Febrile respiratory illness surveillance	No	Yes
Isolation of all patients with acute respiratory symptoms	No	Yes
Awareness of super-spreading events and individuals	No	Yes
Minimizing AGMP and protected intubation policies	No	Yes
Hand hygiene program	No	Yes
Healthy Workplace Policy (work restrictions for HCWs with acute infectious symptoms)	No	Yes
Presence of a pandemic plan	No	Yes
Engineering and environmental controls		
Number of airborne infection isolation room	20 (0 in ED)	46 (8 in ED)
ED infrastructure	Shared air system; no protective barrier at triage	Isolated air system with negative pressure in each zone; protective barrier at triage
Terminal disinfection completed twice at patient discharge for high-consequence pathogen	No	Yes
PPE		
Regular N95 fit-testing of HCWs	No	Yes
Clear recommendation on PPE for any novel high-consequence pathogen	No	Yes

Abbreviations: AGMP, aerosol-generating medical procedure; ED, emergency department; HCW, healthcare worker; ICP, Infection Prevention and Control Professional; IPAC, Infection Prevention and Control; PPE, personal protective equipment.

^aBased on historical local data and the Naylor report [10].

^bSubject to reassessment in the event of a pandemic.

baseline preparedness for novel high-consequence pathogens is that our standard PPE for managing these patients only includes components that are already familiar to our HCWs. This decision was made based on evidence demonstrating that additional PPE complexity is associated with risks of self-contamination during doffing [12]. This approach is also consistent with prior evidence from SARS-CoV-1 suggesting that transmission occurs by the droplet or contact route [13]. Finally, we instituted administrative controls for preventing super-spreading events around AGMP [3, 8]. Although our patient did not end up requiring any AGMP, coordinated communication and planning was in place to ensure these would be performed in a controlled fashion to minimize HCW risk.

When to discharge this patient was a decision that required us to carefully balance the risk that a stable patient who is yet

early in the COVID-19 illness with potential to require medical intervention [2], against the ongoing risk of HCW exposure with each additional day of inpatient care. On the other hand, promoting early discharge of this patient might have resulted in transfer back to hospital if he deteriorated leading to additional risk of exposure during transport. We urgently need to develop evidence-based risk stratification of patients with COVID-19 to determine those best managed at home rather than in hospital as part of our strategy to keeping the number of exposures to a minimum.

How long patients with COVID-19 remain infectious represents a significant gap in our understanding. Our patient's symptoms lasted 12 days, but viral shedding persisted for many days beyond. Current Centers for Disease Control and Prevention and Ontario's Ministry of Health recommendations

are to maintain transmission-based precautions until 2 negative respiratory tract specimens at least 24 hours apart [14], pending more definitive assessment of bioaerosol studies.

Our report has important limitations. First, it represents the experiences of a single healthcare institution and public health unit around a single case, compared to the large number of patients being concurrently managed in the epicenter of the outbreak in Hubei province, China. Second, our patient remained stable and did not require any AGMP, which would have increased the risk of transmission. Finally, our patient presented quite typically and identified based on travel history; however, countries where local transmission has already occurred must rely on syndromic screening alone, which may be more challenging given reports that some patients with COVID-19 may present atypically [2].

In the face of an impending pandemic of COVID-19, the diagnosis and management of this first Canadian case provides hope that we can limit the burden of healthcare-associated infection seen during SARS. We call for scalable and sustainable preparedness for COVID-19 and beyond.

Notes

Acknowledgments. The authors thank all the medical, nursing, environmental services, and laboratory teams that were involved in the patient's care, along with the Senior Leadership Team, Infection Prevention and Control, Microbiology, Emergency Preparedness, Communication and Stakeholder Relations, and Occupational Health & Safety. They also thank their partners outside the hospital: Emergency Services, Public Health Ontario Laboratory, the National Microbiology Laboratory, and the local, provincial, and federal public health agencies. Finally, Dr Mary Vearncombe is thanked for providing historical information on management of SARS.

Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* **2020**; 395:497–506.
2. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. *JAMA* **2020**; 323:1061–9.
3. Raboud J, Shigayeva A, McGeer A, et al. Risk factors for SARS transmission from patients requiring intubation: a multicentre investigation in Toronto, Canada. *PLoS One* **2010**; 5:e10717.
4. Silverstein WK, Stroud L, Cleghorn GE, Leis JA. First imported case of 2019 novel coronavirus to Canada presenting as mild pneumonia. *Lancet* **2020**; 395:734.
5. Corman VM, Müller MA, Costabel U, et al. Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. *Euro Surveill*. **2012**; 17:pii=20334.
6. Corman V, Bleicker T, Brünink S, et al. Diagnostic detection of 2019-nCoV by real-time RT-PCR. Available at: https://www.who.int/docs/default-source/coronaviruse/protocol-v2-1.pdf?sfvrsn=a9ef618c_2 Accessed 12 February 2020.
7. Vijgen L, Moës E, Keyaerts E, Li S, Van Ranst M. A pancoronavirus RT-PCR assay for detection of all known coronaviruses. *Methods Mol Biol* **2008**; 454:3–12.
8. Christian MD, Loutfy M, McDonald LC, et al; SARS Investigation Team. Possible SARS coronavirus transmission during cardiopulmonary resuscitation. *Emerg Infect Dis* **2004**; 10:287–93.
9. Ontario Agency for Health Protection and Promotion (Public Health Ontario), Provincial Infectious Diseases Advisory Committee. Best practices for prevention, surveillance and infection control management of novel respiratory infections in all health care settings. 1st revision. Toronto, ON: Queen's Printer for Ontario; **2020**.
10. Health Canada. Learning from SARS: renewal of public health in Canada – Report of the National Advisory Committee on SARS and Public Health. Ottawa, Canada: Publications Health Canada, **2003**.
11. Puig-Asensio M, Braun BI, Seaman AT, et al. Perceived benefits and challenges of ebola preparation among hospitals in developed Countries: a systematic literature review. *Clin Infect Dis* **2019**; 70:976–86.
12. Mumma JM, Durso FT, Casanova LM, et al. Common behaviors and faults when doffing personal protective equipment for patients with serious communicable diseases. *Clin Infect Dis* **2019**; 69:214–20.
13. Seto WH, Tsang D, Yung RW, et al; Advisors of Expert SARS group of Hospital Authority. Effectiveness of precautions against droplets and contact in prevention of nosocomial transmission of severe acute respiratory syndrome (SARS). *Lancet* **2003**; 361:1519–20.
14. Centers for Disease Control and Prevention. Interim considerations for disposition of hospitalized patients with 2019-nCoV infection. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html>. Accessed 12 February 2020.